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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,894	04/14/2006	Katsuyuki Hamada	56939	4681

1609 7590 05/05/2010

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
05/05/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,894	HAMADA ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9 and 11* is/are pending in the application.

4a) Of the above claim(s) *4-7 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/26/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim amendments filed on 01/28/2010 have been received and entered.

Claims 1, 8, and 10 are cancelled. Claims 2-7, 9, and 11 are pending. Claims 2, 3, and 11 are amended.

Claims 4-7 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 2, 3, and 11 are currently under examination to the extent of elected species 1A1.3B promoter (claim 2), and adenovirus (claim 3).

This application 10/575,894 is a 371 of PCT/JP04/15221 filed on 10/15/2004, which claims the priority of JAPAN 2003-354983, filed on 10/15/2003.

Information Disclosure Statement

It is noted that the non-patent literature (NPL) documents with citation numbers 1 to 6 filed on 02/26/2010 are incomplete because the title of the articles are missing. These NPL documents are considered to the extent of the information documented on the IDS filed on 02/26/2010.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

1. Previous rejection of claims 2, 3, and 11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is ***withdrawn*** because claim 11 has been amended.

Amended claim 11 filed on 01/28/2010 reads as follows: A drug kit for cancer gene therapy therapeutic drug kit comprising: a tumor cell, which is administrated prior to a carrier, cell to perform tumor vaccination, and a carrier cell infected with an oncolytic virus, so as to make the oncolytic virus act on a tumor cell within a living body, wherein the carrier cell is a A549 cell.

Claims 2 and 3 depend from claim 11.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 2, 3, and 11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Nanni et al.** (Nanni et al., Combined allogeneic tumor cell vaccination and systemic interleukin 12 prevents mammary carcinogenesis in HER-2/neu transgenic mice, J Exp Med. 2001 Nov 5;194(9):1195-205, 2001) in view of **Hamada et al.** (Hamada et al., Identification of the human IAI.3B promoter element and its use in the construction of a replication-selective adenovirus for ovarian cancer therapy, *Cancer Res.* 63(10):2506-12, 2003; this reference has been cited in the office action mailed on 09/04/2008). Applicant's arguments filed 01/28/2010 have been fully

considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 6-10 of the office action mailed on 09/29/2009.

For the clarity and completeness of this office action, the rejection for the reasons of record advanced on pages 6-10 of the office action mailed on 09/29/2009 is reiterated below, with revisions addressing claim amendments filed on 01/28/2010.

Applicant's arguments and Examiner's ***Response to Applicant's arguments*** are addressed collectively at the end of maintained two 103 rejections in this office action.

Amended claim 11 filed on 01/28/2010 reads as follows: A drug kit for cancer gene therapy therapeutic drug kit comprising: a tumor cell, which is administrated prior to a carrier, cell to perform tumor vaccination, and a carrier cell infected with an oncolytic virus, so as to make the oncolytic virus act on a tumor cell within a living body, wherein the carrier cell is a A549 cell.

Claim 2 further limits claim 11 by recitation of the oncolytic virus to be infected to the carrier cell has the 1A1.3B promoter.

Claim 3 further limits claim 11 by recitation of the virus for immunological treatment and the oncolytic virus being adenovirus.

Claim interpretation: **(i)** The limitation "a tumor cell, which is administrated prior to a carrier" recited in line 2 of claim 11 is not necessarily the same tumor cell encompassed by "a tumor cell within a living body" recited in lines 4-5 of claim 11 as written. **(ii)** It is noted that, for prior art rejection of a product, the components of the product are considered for patentable weight whereas intended uses of the product, bear limited, patentable weight, if any. For claim 11, the phrases "which is administrated prior to a carrier cell to perform tumor vaccination" and "so as to make the oncolytic virus act on a tumor cell within a living body" are considered as intended uses of the claimed drug kit. For the same reason, the intended use "for immunological treatment" recited in line 2 of claim 3 is considered for limited patentable weight, if any.

The above claim interpretations are based on MPEP 2111.03 cited below.

The intended use and inherent properties are not considered with patentable weight for the claimed composition because the components of the composition remain the same. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

With regard to a tumor cell for intended use in tumor vaccination recited in claim 11, **Nanni et al.** teaches administering allogeneic mammary carcinoma cells expressing HER-2/neu combined with systemic IL-12. This treatment reduced tumor incidence by 90% and more than doubled mouse lifetime. For the maximum prevention p185 (neu) antigen must be expressed by allogeneic cells, and IL-12 treatment strongly increased the cell vaccine efficacy (See abstract, Nanni et al., 2001).

With regard to the limitation "A549 cell" recited in claim 11, the limitation "IAI.3B promoter" recited in claim 2, and adenovirus recited in claim 3, **Hamada et al.** disclosed the following teachings : **(i)** Identification of the tissue specific promoter region of the IAI.3B gene and construction of a replication-selective adenovirus, AdE3-*IAI.3B*, driven by the promoter (See abstract and Figure 2, Hamada et al., 2003); **(ii)** The lung cancer A549 transfected with an

oncolytic adenovirus Ad*E2F-1*^{RC}, and AdE3-*IAI.3B* has a construction design similar to that of the adenovirus Ad*E2F-1*^{RC}, because both have an intact *E1A* promoter upstream of their respective heterologous promoters (See Discussion, second paragraph, right column, page 2510, Hamada, 2003), and **(iii)** AdE3-*IAI.3B* replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of ovarian cancer cells *in vitro*, in contrast, squamous cell carcinoma and normal cells were not able to support AdE3-*IAI.3B* replication (See abstract and Figure 3, Hamada et al., 2003), and **(iv)** In animal studies, AdE3-*IAI.3B* administered to flank and i.p. xenografts of ovarian cancer cells led to a significant therapeutic effect (See abstract and Figure 4, Hamada et al., 2003).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Nanni et al. regarding administering allogeneic mammary carcinoma cells expressing HER-2/neu for breast cancer vaccination, with the teachings of Hamada et al. regarding identification of the human IAI.3B promoter element and its use in the construction of a replication-selective adenovirus for ovarian cancer therapy, to arrive at a kit comprising a tumor cell for tumor vaccination and the A549 cell infected with an oncolytic adenovirus for killing ovarian tumor cells, as recited in claims 2, 3, and 11 of instant application.

One having ordinary skill in the art would have been motivated to combine the teachings of Nanni et al. and Hamada et al. because there are two different molecular mechanisms underlying the treatment of breast and ovarian cancers. In this regard, Nanni et al. teaches administering allogeneic mammary carcinoma cells expressing HER-2/neu for breast cancer vaccination to enhance immune response against the cancer cells whereas Hamada et al. teaches

replication-selective oncolytic adenovirus comprising by IAI.3B promoter that targets ovarian cancer specifically.

There would have been a reasonable expectation of success given (i) the immune response against breast cancer antigen HER-2/neu elicited by the administration allogeneic mammary carcinoma cells expressing HER-2/neu, by the teachings of Nanni et al., and (ii) successful demonstration of AdE3-*IAI.3B* replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of ovarian cancer cells *in vitro*, in contrast, squamous cell carcinoma and normal cells were not able to support AdE3-*IAI.3B* replication, by the teachings of Hamada et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

3. Claims 2, 3, and 11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Nanni et al.** (Nanni et al., Combined allogeneic tumor cell vaccination and systemic interleukin 12 prevents mammary carcinogenesis in HER-2/neu transgenic mice, J Exp Med. 2001 Nov 5;194(9):1195-205, 2001) in view of **Tsukuda et al.** (Tsukuda et al., An E2F-responsive replication-selective adenovirus targeted to the defective cell cycle in cancer cells: potent anti-tumoral efficacy but no toxicity to normal cell. *Cancer Res.* 62(12):3438-47, 2002; this reference has been cited in the office action mailed on 09/04/2008) and **Barker et al.** (Barker et al., WO 98/23779, international publication date, 06/04/1999). Applicant's arguments filed 01/28/2010 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 10-15 of the office action mailed on 09/29/2009.

For the clarity and completeness of this office action, the rejection for the reasons of record advanced on pages 10-15 of the office action mailed on 09/29/2009 is reiterated below, with revisions addressing claim amendments filed on 01/28/2010.

Amended claim 11 filed on 01/28/2010 reads as follows: A drug kit for cancer gene therapy therapeutic drug kit comprising: a tumor cell, which is administrated prior to a carrier, cell to perform tumor vaccination, and a carrier cell infected with an oncolytic virus, so as to make the oncolytic virus act on a tumor cell within a living body, wherein the carrier cell is a A549 cell.

Claim 2 further limits claim 11 by recitation of the oncolytic virus to be infected to the carrier cell has the 1A1.3B promoter.

Claim 3 further limits claim 11 by recitation of the virus for immunological treatment and the oncolytic virus being adenovirus.

Claim interpretation: **(i)** The limitation "a tumor cell, which is administrated prior to a carrier" recited in line 2 of claim 11 is not necessarily the same tumor cell encompassed by "a tumor cell within a living body" recited in lines 4-5 of claim 11 as written. **(ii)** It is noted that, for prior art rejection of a product, the components of the product are considered for patentable weight whereas intended uses of the product, bear limited, patentable weight, if any. For claim 11, the phrases "which is administrated prior to a carrier cell to perform tumor vaccination" and "so as to make the oncolytic virus act on a tumor cell within a living body" are considered as intended uses of the claimed drug kit. For the same reason, the intended use "for immunological treatment" recited in line 2 of claim 3 is considered for limited patentable weight, if any.

The above claim interpretations are based on MPEP 2111.03 cited below.

The intended use and inherent properties are not considered with patentable weight for the claimed composition because the components of the composition remain the same. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

With regard to a tumor cell for intended use in tumor vaccination recited in claim 11, **Nanni et al.** teaches administering allogeneic mammary carcinoma cells expressing HER-2/neu combined with systemic IL-12. This treatment reduced tumor incidence by 90% and more than doubled mouse lifetime. For the maximum prevention p185 (neu) antigen must be expressed by allogeneic cells, and IL-12 treatment strongly increased the cell vaccine efficacy (See abstract, Nanni et al., 2001).

With regard to the limitation "A549 cell" recited in claim 1, the limitation "1A1.3B promoter" recited in claim 2, and adenovirus recited in claim 3, **Tsukuda et al.** disclosed the following teachings : **(i)** The construction of an adenovirus Ad*E2F-1*^{RC} and transfection of the Ad*E2F-1*^{RC} in A549 cells, so that E1A expression and viral replication were under the control of the human E2F-1 promoter element (See abstract and Material and Methods, left column, page 3440, Tsukuda et al., 2002); **(ii)** The Ad*E2F-1*^{RC} virus replicated as efficiently as the wild-

type adenovirus and caused extensive cell killing in a panel of tumor cells (i.e. an oncolytic virus) *in vitro*, in contrast, non-proliferating normal epithelial, fibroblast, and endothelial cells, which express no E2F-1, were not able to support Ad*E2F-1*^{RC} replication (See abstract and Figures 3-5, Tsukuda et al., 2002); and **(iii)** In animal studies, different dosing regimens of Ad*E2F-1*^{RC} administered to flank xenografts of ovarian and lung cancers led to a significant therapeutic advantage often surpassing that seen in animals treated with the wild-type adenovirus (See abstract and Figures 6-7, Tsukuda et al., 2002). Furthermore, **Barker et al.** teaches IAI.3B promoter and BRCA1 promoter are involved in breast and ovarian cancer etiology (See abstract and Example 4 on pages 19-20, Baker et al., 1998). It is noted that replacing E2F promoter taught by Tsukuda et al. with the IAI.3B promoter taught by Baker et al. would result in tissue specificity infection of the adenovirus with reasonable expectation of success because swapping promoters to achieve tissue specific expression of a gene of interest is a well-established molecular technique to a skilled artisan.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Nanni et al. regarding administering allogeneic mammary carcinoma cells expressing HER-2/neu for breast cancer vaccination, with the teachings of Tsukuda et al. regarding administration of A459 cells infected with mutated oncolytic adenovirus Ad*E2F-1*^{RC} results to killing of variety of cancer cells, and the teachings of Baker et al. regarding involvement of IAI.3B promoter is involved in breast and ovarian cancer etiology, to arrive at a kit comprising a tumor cell for tumor vaccination and the A549 cell infected with an oncolytic adenovirus for killing tumor cells, as recited in claims 2, 3, and 11 of instant application.

One having ordinary skill in the art would have been motivated to combine the teachings of Nanni et al., Hamada et al., and Barker et al. because there are two different molecular mechanisms involved in treating breast and ovarian cancer etiology. In this regard, Nanni et al. teaches administering allogeneic mammary carcinoma cells expressing HER-2/neu for breast cancer vaccination to enhance immune response against the cancer cells whereas combined teachings of Tsukuda et al. and Baker et al. teach replication-selective oncolytic adenovirus comprising the IAI.3B promoter that targets ovarian cancer specifically.

There would have been a reasonable expectation of success given (i) the immune response against breast cancer antigen HER-2/neu elicited by the administration allogeneic mammary carcinoma cells expressing HER-2/neu, by the teachings of Nanni et al., and (ii) successful demonstration of treating cancer cells A459 cells infected with replication-selective oncolytic adenovirus Ad*E2F-1*^{RC} leads to potent anti-tumoral efficacy but no toxicity to normal cells by the teachings of Tsukuda et al., and (iii) the disclosure of IAI.3B promoter being active specifically in breast cancer and ovarian cancer cells, by the teachings of Barker et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Applicant's arguments

Applicant argues that the kit in claim 11 is not just a carrier cell (A549 cell) but a combination of a carrier cell and a tumor cell; and the remarkable result achieved by administrating a tumor cell and an adenovirus-infected A549 cell.

Applicant states that Nanni et al. does not disclose carrier cells, and Hamada or Tsukuda do not disclose administrating a tumor cell to perform tumor vaccination. KSR does not allow the mere picking of items from a shopping list disclosed in the application to make a 103 rejection. Although KSR may have lowered the standard for citing references for a 103 rejection,

KSR still requires a showing that it would have been "obvious to try" the claimed combination of items by a person skilled in the art. The Office Action fails to cite any disclosure in the references to support the alleged "obvious to try".

Applicant states that, in KSR, the court quoting In re Kahn (Fed Cir 2006) (Page 15, second paragraph), stated that "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." Therefore, the Examiner is requested to clearly articulate the reason(s) why the claimed "drug kit for cancer gene therapy" would have been obvious to try by a person skilled in the art after reading the cited references. The Office Action fails to state how a person skilled in the art would know to combine the claimed specific items in a kit to achieve the disclosed superior results. It is only after the disclosure of this application that a person skilled in the art would think of combining Hamada et al. or Tsukuda et al. with Nanni et al. This selection of references in order to obtain the claimed items in the kit has been accomplished by hindsight; which is improper for making a 103 rejection.

Applicant states that even though Hamada and Tsukuda disclose a A549 cell, the main findings of these references is a replication-selective adenovirus for cancer therapy. However, these references do not disclose any reason to combine a A549 cell with a tumor cell.

Applicant states that, additionally, as shown in paragraph [0168] of the present specification and Fig. 22 (a) and (b), tumors completely disappeared in mice by tumor vaccination followed by adenovirus- infected A549 cells. This result is much superior when compared with only administering a carrier cell adenovirus-infected A549 cell. The superior synergetic result due to the combined use of a tumor cell and a A549 cell (carrier cell) when compared to the use of a carrier cell alone shows unexpected results, which demonstrate the lack of the "obvious to try" standard.

Applicant argues that Barker only teaches the IAI.3B promoter and BRACA1 promoter are involved in breast and ovarian cancer, however it does not disclose a carrier cell or tumor vaccination.

Applicant concludes that, therefore, the kit in Claim 11 is unobvious over Nanni et al., in

view of Tsukuda et al. and Barker et al. Claims 2 and 3 depend from Claim 11 and thus these claims are also unobvious over the cited references.

Response to Applicant's arguments

It is worth noting that the calimed kit is a product comrpising a tumor cell and a carrier cell as recited in claim 11, not a method for treating cancers, which is the intended use of claimed kit. For prior art rejection, if the prior art structure is capable of performing the intended use, then it meets the claim. Applicant's statement that "Hamada and Tsukuda disclose a A549 cell" appears to indicate that Applicant acknowledges that there is no structural distinction between claimed product and the product taught by recited prior arts. In this regard, it is worth noting that Applicant's arguments filed on 01/28/2010 fail to provide any evidence that the claimed products are *structurally distinct* and non-obvious as compared to the products taught in the prior art. Consistently, the Examiner had noted in the interveiw summary mailed on 12/31/2009 that Hamada et al. (Cancer Research 63: 2506-2512, 2003) is Applicant's own publication with a 102(b) date.

Additionally, as stated in the maintained rejection, the following claim interpretations apply to this rejection: **(i)** The limitation "a tumor cell, which is administrated prior to a carrier" recited in line 2 of claim 11 is not necessarily the same tumor cell encompassed by "a tumor cell within a living body" recited in lines 4-5 of claim 11 as written. **(ii)** It is noted that, for prior art rejection of a product, the components of the product are considered for patentable weight whereas intended uses of the product, bear limited, patentable weight, if any. For claim 11, the phrases "which is administrated prior to a carrier cell to perform tumor vaccination" and "so as to make the oncolytic virus act on a tumor cell within a living body" are considered as intended uses of the claimed drug kit. For the same reason, the intended use "for immunological treatment" recited in line 2 of claim 3 is considered for limited patentable weight, if any.

Furthermore, as stated in the maintained rejection, one having ordinary skill in the art would have been motivated to combine the teachings of Nanni et al. and Hamada et al. because there are two different molecular mechanisms underlying the treatment of breast and ovarian cancers. In this regard, Nanni et al. teaches administering allogeneic mammary carcinoma cells

expressing HER-2/neu for breast cancer vaccination to enhance immune response against the cancer cells whereas Hamada et al. teaches replication-selective oncolytic adenovirus comprising by IAI.3B promoter that targets ovarian cancer specifically.

There would have been a reasonable expectation of success given (i) the immune response against breast cancer antigen HER-2/neu elicited by the administration allogeneic mammary carcinoma cells expressing HER-2/neu, by the teachings of Nanni et al., and (ii) successful demonstration of AdE3-*IAI.3B* replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of ovarian cancer cells *in vitro*, in contrast, squamous cell carcinoma and normal cells were not able to support AdE3-*IAI.3B* replication, by the teachings of Hamada et al.

With regard to Applicant's arguments that argument that though Hamada and Tsukuda disclose a A549 cell disclose a A549 cell, the main findings of these references is a replication-selective adenovirus for cancer therapy, however, these references do not disclose any reason to combine a A549 cell with a tumor cell, the Examiner would like to direct Applicant's attention to recent decision by U.S. Supreme Court in *KSR International Co. v. Teleflex, Inc.* that forecloses the argument that a **specific** teaching, suggestion, or motivation is an absolute requirement to support a finding of obviousness. See recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1936) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf). The Examiner notes that in the instant case, even in the absence of recent decision by U.S. Supreme Court in *KSR International Co. v. Teleflex, Inc.,* the suggestion and motivation to combine Nanni et al. and Hamada (as well as combine Nanni et al., Tsukuda et al., and Barker et al.) has been clearly set forth above in this office action in the context of two different molecular mechanisms underlying the treatment of breast and ovarian cancers, which is the reason why the Examiner does not apply "obvious to try" rational under KSR.

Finally, it is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30

PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Primary Examiner
Art Unit 1632